CLAIMS

Claim 1 (original): A method of treating a disease or disorder characterized by high intracellular calcium levels in an individual in need thereof, comprising:

providing an effective amount of an opener of maxi-K potassium channels to said individual, wherein said opener activates maxi-K potassium channels in cells under conditions of high intracellular calcium concentration, and does not significantly activate maxi-K potassium channels in cells under low or normal concentrations of intracellular calcium.

Claim 2 (original): The method according to claim 1, further wherein influx or introduction of additional calcium into cells having high intracellular calcium concentration is restricted or reduced.

Claim 3 (original): The method according to claim 1, wherein the disease or disorder is a neurodegenerative disease or disorder.

Claim 4 (original): The method according to claim 3, wherein the neurodegenerative disease or disorder is selected from the group consisting of stroke, global cerebral ischemia, traumatic brain injury, Parkinson's disease, epilepsy, migraine and Alzheimer's disease.

Claim 5 (original): The method according to claim 4, wherein the neurodegenerative disease is stroke.

Claim 6 (original): The method according to claim 5, wherein the neurodegenerative disease is ischemic stroke or acute ischemic stroke.

Claim 7 (original): The method according to claim 6, wherein the cells having a high intracellular calcium concentration are preischemic or ischemic neurons.

Claims 8 (original): The method according to claim 1, wherein the maxi-K potassium channel opener is selected from the group consisting of fluoro-oxindole compounds and chloro-oxindole compounds.

Claim 9 (original): The method according to claim 8, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 10 (original): The method according to claim 9, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 11 (original): The method according to claim 8, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

Claim 12 (original): The method according to claim 1, wherein the maxi-K potassium channel opener is administered prior to or following the onset of the disease or disorder.

13. The method according to claim 5 or claim 6, wherein the maxi-K potassium channel opener is administered prior to or following the onset of stroke, ischemic stroke, or acute ischemic stroke.

Claim 14 (original): A method of treating stroke in an individual in need thereof, comprising:

administering to the individual an effective amount of a maxi-K channel opener, said opener having opener activity on maxi-K potassium channel proteins in neuronal cells having a high intracellular calcium concentration, while having no significant opener activity on maxi-K potassium channel proteins in neuronal cells having normal or low intracellular calcium concentration.

Claim 15 (original): The method according to claim 14, wherein the maxi-K channel opener is selected from the group consisting of fluoro-oxindole compounds and chloro-oxindole compounds.

Claim 16 (original): The method according to claim 15, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 17 (original): The method according to claim 16, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 18 (original): The method according to claim 15, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

Claim 19 (original): The method according to claim 14, wherein ischemic is stroke or acute ischemic stroke is treated.

Claim 20 (original): The method according to claim l4 or claim 19, wherein the maxi-K channel opener is administered prior to or following the onset of stroke, ischemic stroke or acute ischemic stroke.

Claim 21 (original): The method according to claim 14, wherein the maxi-K channel opener provides cortical neuroprotection by restricting entry of calcium into neuronal cells exposed to toxic levels of calcium.

Claim 22 (original): A method of treating a disease or disorder characterized by high intracellular calcium levels in an individual in need thereof, comprising:

a) providing to the individual an opener of maxi-K channels wherein the opener is sensitive to high intracellular calcium concentration and targets maxi-K channels in cells associated with the disease or disorder and having high intracellular calcium concentration, while not significantly targeting cells having low or normal intracellular calcium concentration; and

b) reducing or restricting influx of additional calcium into the cells associated with the disease or disorder, increasing potassium efflux and regulating membrane potential, thereby protecting the cells associated with the disease or disorder from toxicity or death.

Claim 23 (original): The method according to claim 22, wherein the maxi-K channel opener is a fluoro-oxindole compound or a chloro-oxindole compound.

Claim 24 (original): The method according to claim 23, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 25 (original): The method according to claim 24, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 26 (original): The method according to claim 24, wherein the fluoro-oxindole compound is (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 27 (original): The method according to claim 23, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-rnethoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one.

Claim 28 (original): The method according to claim 22, wherein the disease or disorder is a neurodegenerative disease or disorder.

Claim 29 (original): The method according to claim 28, wherein the neurodegenerative disease or disorder is selected from the group consisting of stroke, global cerebral ischemia, traumatic brain injury, Parkinson's disease, epilepsy, migraine and Alzheimer's disease.

Claim 30 (original): The method according to claim 29, wherein the neurodegenerative disease or disorder is stroke.

Claim 31 (original): The method according to claim 30, wherein the neurodegenerative disease or disorder is ischemic stroke or acute ischemic stroke.

Claim 32 (original): The method according to claim 22, wherein the cells associated with the disease or disorder and having a high intracellular calcium concentration are at-risk preischemic neurons or ischemic neurons.

Claim 33 (original): The method according to claim 29, wherein the neurodegenerative disease or disorder is traumatic brain injury.

Claim 34 (original): The method according to claim 22, wherein the maxi-K channel opener is administered prior to or after the onset of the disease or disorder.

Claim 35 (original): A method of providing neuroprotection from stroke in an individual in need thereof, comprising: administering an effective amount of a maxi-K potassium channel opener compound that activates maxi-K potassium channel proteins in neurons having a high intracellular calcium concentration, while having no significant opener activity on maxi-K potassium channel proteins in neurons having low or normal intracellular calcium concentration.

Claim 36 (original): A method of providing neuroprotection from stroke in an individual in need thereof, comprising: administering an effective amount of a fluoro-oxindole or chloro-oxindole compound to the individual wherein the compound is a maxi-K potassium channel opener compound that activates maxi-K potassium channel proteins in neurons having a high intracellular calcium concentration, while having no significant opener activity on maxi-K

potassium channel proteins in neurons having low or normal intracellular calcium concentration, thereby providing cortical neuroprotection by restricting entry of calcium into the neurons at risk for neurotoxicity or death.

Claim 37 (original): The method according to claim 35 or claim 36, wherein the maxi-K channel opener compound is a fluoro-oxindole compound.

Claim 38 (original): The method according to claim 37, wherein the fluoro-oxindole compound is selected from the group consisting of (±)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one; and (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 39 (original): The method according to claim 38, wherein the fluoro-oxindole compound is (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 40 (original): The method according to claim 38, wherein the fluoro-oxindole compound is (3S)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indole-2-one.

Claim 41 (original): The method according to claim 35 or claim 36, wherein the maxi-K channel opener compound is a chloro-oxindole compound.

Claim 42 (original): The method according to claim 41, wherein the chloro-oxindole compound is selected from the group consisting of (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2 H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one; and (3R)-(-)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-chloro-6-(trifluoromethyl)-2H-indol-2-one.

Claim 43 (original): The method according to claim 35 or claim 36, wherein the maxi-K channel opener compound is administered prior to or after the onset of stroke.